CEP Clin Exp Pediatr Vol. 65, No. 6, 302-303, 2022
https://doi.org/10.3345/cep.2022.00283

Coronavirus disease 2019 and mRNA vaccines: what's next – miRNA?

To the editor

The coronavirus disease 2019 (COVID-19) pandemic, which began in late 2019 to early 2020, continues. Multiple countermeasures against the COVID-19 pandemic have been implemented. Until now, vaccines against COVID-19 have been generally accepted as the core element of exit strategies despite some disappointment since herd immunity, which was initially expected, could not be achieved. The first COVID-19 vaccine brought to market was a novel messenger RNA (mRNA)-based vaccine manufactured by Pfizer, Inc.[1] We have since become familiar with mRNA vaccines, as a large number of people have been vaccinated with the Pfizer vaccine or the vaccine manufactured by Moderna, Inc. However, societies did not benefit significantly from accumulated knowledge in the field of mRNA until the COVID-19 pandemic.

For pediatricians, the relatively mild symptoms of COVID-19 in children and adolescents are a relief to some extent. Instead, issues about COVID-19 vaccines have arisen as major challenges for pediatricians, starting from fundamental questions such as whether to give vaccine shots to appropriate pediatric age groups. Recent studies have shown that children with comorbidities have a higher prevalence of severe COVID-19 infection; thus, vaccinations are recommended for certain groups.[2] For adolescents, however, myocarditis following mRNA vaccines has become a major problem.[3] Mainly in male adolescents and young adults, myocarditis has been reported more frequently than expected following the receipt of mRNA vaccines. As this was not observed after non-mRNA vaccines, although the pathogenic mechanism has not yet been revealed, the mRNA vaccine platform seems associated with adverse events.

Myocarditis is an inflammatory myocardial disease. Its causes are diverse and include infectious, toxic, and autoimmune etiologies.[4] Despite the widespread use of nucleic acid amplification tests, definite etiologic agents are not always elucidated. Furthermore, considering the limitations of specific antivirals for identified pathogens and the nearly uniform strategies in the management of myocarditis, the confirmation of each etiologic pathogen might have lower value than expected. Despite advances in the management of myocarditis, which includes but is not limited to hemodynamic support, arrhythmia management, anticoagulation, and immunomodulatory therapy, mortality rates during acute illness in children with myocarditis are 5%–15%.[5] Furthermore, approximately 5%–20% of children with acute myocarditis require heart transplantation.[6] A large knowledge gap still remains regarding the optimal management of myocarditis. To compensate for this knowledge gap, biomarkers are invaluable, especially in myocarditis, for which procedures such as endomyocardial biopsy carry risks, particularly in young children and those who are critically ill.

The review article by Oh et al.[7] provides a completely new perspective. The authors performed a comprehensive review of the basic information and recent research highlights about disease-specific microRNA (miRNA) expression patterns as a potential novel biomarker of cardiac disease, including myocarditis. These miRNAs are small single-stranded noncoding RNA molecules (containing approximately 22 nucleotides) found in plants, animals, and some viruses that function in RNA silencing and the posttranscriptional regulation of gene expression.[8] As described in the review article, miRNA expression profiling studies have demonstrated that the expression levels of specific miRNAs change in diseased human hearts, pointing to their involvement in cardiomyopathies. However, the clinical application of miRNAs is extremely limited, as they degrade much more easily than mRNAs, partly because of their length but also because of ubiquitous RNAses.[9]

Because miRNAs are involved in the normal functioning of eukaryotic cells, their dysregulation is associated with disease. As such, studies of miRNAs in association with various diseases and fields continue. For example, the first human disease associated with deregulation of miRNAs was chronic lymphocytic leukemia, in which miRNAs have a dual role as both tumor suppressors and oncogenes.[10] Other areas in which miRNAs are being actively studied include cancer, kidney disease, nervous system disease (such as neurodegenerative disease and stroke), obesity, and severe acute respiratory syndrome coronavirus 2.

The ongoing pandemic has left light and shadows. Accumulated basic science knowledge in the field of mRNA has provided humankind with a tool against COVID-19. Many researchers are immersing themselves in miRNA study despite limited social interest. As with mRNA, some miRNAs may become solutions for catastrophes. Until then, interest in miRNA in terms of one's own area of expertise might be of value.

See the article "Implication of microRNA as a potential biomarker of myocarditis" via https://doi.org/10.3345/cep.2021.01802.

Received: 29 October 2021, Revised: 7 April 2022, Accepted: 13 April 2022

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Key message

MicroRNAs (miRNAs) are small single-stranded noncoding RNA molecules that function in RNA silencing and the posttranscriptional regulation of gene expression. The potential role of miRNAs as biomarkers of myocarditis is promising, and miRNAs are expected to be utilized in various clinical fields in the future.

Footnotes

Conflicts of interest: No potential conflict of interest relevant to this article was reported.

Funding: This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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How to cite this article: Lee JK, Han HS. Coronavirus disease 2019 and mRNA vaccines: what's next – miRNA? Clin Exp Pediatr 2022;65:302-3. https://doi.org/10.3345/cep.2022.00283